UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/532,831 | 03/09/2006 | Hans-Ulrich Petereit | 267336US0PCT | 8866 |

22850 7590 04/16/2008

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

| EXAMINER | |
|---|---|
| WESTERBERG, NISSA M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1618 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 04/16/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/532,831 | PETEREIT ET AL. | |
| | Examiner | Art Unit | |
| | Nissa M. Westerberg | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 - 12* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :4/26/05; 9/16/05; 3/29/06; 12/12/06; 12/13/07.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of 5-aminosalicylic acid in the reply filed on February 11, 2008 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

### *Claim Rejections - 35 USC § 112 2nd Paragraph*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 – 9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The inner coating is described as consisting substantially of a methacrylate copolymer and comprising the pharmaceutical active substance in bound form. It is unclear if the active substance is bound to the methacrylate copolymer itself and both are present in the same layer or if the active substance is bound to the methacrylate copolymer layer and the inner coating itself has multiple layers.

4. Claims 1 – 9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The composition of the polymer in coating in each layer is defined, but the amount of that polymer present in relation to the other ingredients in the layer is only defined by the phrase "substantially of". This term is a relative term which renders the claim indefinite. The term "substantially of" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

5. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In one interpretation, the outer coating can be a combination of methacrylic acid and methyl methacrylate or it can consist substantially of ethyl acrylate. The other interpretation is that methacrylic acid must be present in combination with either methyl methacrylate or ethyl methacrylate.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 3 – 6, 8, 9, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ulmius (US Patent 5,643,602).

Ulmius discloses multilayer compositions of corticosteroids such as budesonide (col 3, ln 6; col 4, ln 50). Each unit comprises a core and two layers on that core (col 5, ln 3 – 4). The core can either be formulated with the glucocorticosteroid homogenously

throughout the core or the active ingredient can be applied to the exterior of the seed (col 5, ln 5 – 8). When the drug is applied to the seed, the drug is applied in combination with a polymer that acts as a binder for the active ingredient and to limit the release rate (col 5, ln 12 – 16). Preferred film-forming polymers are ethylcellulose or copolymers of acrylic and methacrylic acid esters such as the compounds sold under the tradenames EUDRAGIT® NE, EUDRAGIT® RL and EUDRAGIT® RS (col 5, ln 24 – 26). EUDRAGIT® NE 30D is a polymer that meets the monomer requirements for the inner coating in claims 1 and 2 as it contains 65 wt% ethyl acrylate and 35% wt% methyl methacrylate (p 26, ln 10 – 12 of the instant application). The ratio of the active ingredient to the polymer is 1:6.6 and 1:2.4 in examples 1 and 2 respectively (col 8, ln 24 – 30; col 9, ln 14 – 20). The film-forming temperature of the polymer is determined by the composition of the polymer and as the composition of the polymers are the same, the film-forming temperature of the polymer will meet the limitations put forth in the claim.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

The second layer polymer can be selected from those polymers that are soluble at a higher pH but is only soluble with difficulty at a low pH (col 5, ln 33 – 38). The

polymers preferred for this layer are acrylic acid polymers such as the partly esterified methacrylic acid polymers EUDRAGIT® L, EUDRAGIT® L100-55 and EUDRAGIT® S series (col 5, ln 40 – 47).

The EUDRAGIT® L and L 100-55 series polymers meet the limitations for the outer layer polymer presented in both claims 1 and 4 as they comprise 40 to 60 wt% methacrylic acid and 60 to 40 wt% methyl methacrylate or 60 to 40 wt% ethyl acrylate (p 19, ln 38 – p 20, ln 3 of the instant application).

The EUDRAGIT® S series polymers meet the limitations for the outer layer polymer presented in claims 1, 5 and 6 as they comprise 20 to 40 wt% methacrylic acid and 80 to 60 wt% methyl methacrylate (p 20, ln 5 - 8 of the instant application). As to the glass transition temperature, this property is determined by the composition of the polymer and as the prior art teaches a composition with the same monomer composition as required in the instant claim, the composition of the prior art will also meet the requirement for the glass transition temperature set forth in claim 6.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

In the examples, AQUACOAT® ECD 30 (ethylcelluose) is used as the polymer on the inner layer with budesonide as the active ingredient over an inert core and coated with a layer comprising various EUDRAGIT® polymers.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to replace the ethylcellulose with the equally preferred EUDRAGIT® series of polymers as the binder for the active agent that coats a neutral core, resulting in the multilayer dosage form of the claims of the instant application. The release rate of the active substance are determined by the composition of the multilayer dosage form and as the prior art teaches a composition as claimed by Applicant, the composition of the prior art necessarily provides the same (no difference by more than 10% within 1 – 5 hours) release of the active substance.

10. Claims 1 – 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ulmius (US Patent 5,643,602) in view of Beckert et al. (WO 01/68058; citations from the English language equivalent PGPub 2002/0192282).

As discussed above, Ulmius discloses a multilayer dosage form of corticosteroids such as budesonide. These dosage forms are intended to be used in the treatment of inflammatory bowel disease (col 1, ln 13 – 15). The release profile of the active ingredient should be such that no release occurs in the stomach but is released in either the small intestine when Crohn's disease is being treated or is released over an even longer time in order to deliver the active agent to the cecum and colon (col 4, ln 23 – 49).

Ulmius does not disclose any other active ingredients besides glucocorticosteroids as suitable for use in such compositions. Ulmius also does not disclose the use of a polymer that meets the limitations for the inner coating required in claim 2 or an outer coating layer required in claim 7.

Beckert et al. discloses a multilayer drug form with a core and both an inner and outer polymer coatings (paragraph [0001]). This dosage form is designed to release virtually no active ingredient in the stomach and have a uniform, long-lasting release of the active ingredient to both the small intestine and colon (paragraph [0006]). A number of active ingredients are suitable for use in these compositions, including budesonide (paragraph [0043]), but also aminosalicylates such as 5-aminosalicyclic acid, sulfonamides and glucocorticosteroids (paragraphs [0032] – [0034]).

Beckert et al. states that suitable polymers for the inner coating are disclosed in EP-A 1 181 515 (English language equivalent US Patent 4,737,357). Among the polymers disclosed therein are copolymers ethyl acrylate, methyl methacrylate and methacryloxyethyltrimethylammonium chloride wherein the weight ratios of the components are 60:35:10 or 65:35:5 (col 2, ln 50 – 58). Methacryloxyethyltrimethylammonium chloride is a vinylically polymerizable monomer and therefore the polymers disclosed meet the limitations for the inner coating of the multilayer dosage form in claim 2 of the instant application.

Beckert et al. discloses that a particularly suitable polymer for the outer coating of the multilayer pharmaceutical formulation is a (meth)acrylate copolymer composed of 10 – 30 wt% methyl methacrylate, 50 to 70 wt% methyl acrylate and 5 to 15 wt%

methacrylic acid (EUDRAGIT® FS type; paragraph [0087]). These match the limitations for the outer layer polymer recited in claim 7 of the instant application.

It would have been obvious to one of ordinary skill in the art to replace the budesonide designed for delivery to the small intestine and/or colon in the multilayer dosage form taught by Ulmius with other active agents such as 5-aminosalicylate that are also targeted for the small intestine and colon as taught by Beckert et al. It also would have been obvious to use a EUDRAGIT® FS type polymer as the outer coating and the ethyl acrylate and methyl methacrylate copolymer for the inner coating in the multilayer dosage form as both Ulmius and Beckert et al. teach multilayer dosage forms with a core and two coating layers that release virtually no active substance in the stomach and deliver the active agent to the small intestine or colon. While the multilayer dosage form of Beckert et al. contains the active ingredient in the core, Ulmius discloses that the active ingredient can either be included in the core or in the first layer that is coated onto that core.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW